PRVD2009-02

Proposed Re-evaluation Decision

Quintozene

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Overview

What Is the Proposed Re-evaluation Decision?

After a re-evaluation of the fungicide quintozene, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration of certain products containing quintozene for the sale and use in Canada.

Products containing quintozene used on cole crops and for ornamental bulb dip treatments do not pose unacceptable risk to human health or the environment, and have value for agriculture when used according to the label directions. As a condition for continued registration of quintozene products, new risk-reduction measures will be required on product labels. In addition, the registrant must submit additional data as identified in this document.

Certain uses of quintozene are proposed for phase-out because the risk associated with these uses exceeds current health and environmental standards. They include all uses on turf and ornamentals (except bulb dip treatment).

Once the final re-evaluation decision is made, the registrants will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision (PRVD) is a consultation document[1] that summarizes the science evaluation for quintozene and presents the reasons for the proposed re-evaluation decision.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the assessment of quintozene.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (see contact information indicated on the cover page of this document).

What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure.

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[1] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

Quintozene, one of the active ingredients in the current re-evaluation cycle, has been re-evaluated under Re-evaluation Program 1. This program relies as much as possible on foreign reviews, typically the United States Environmental Protection Agency (USEPA) Reregistration Eligibility Decision (RED) documents. For products to be re-evaluated under Program 1, the foreign review must meet the following conditions:

- it covers the main science areas, such as human health and the environment, which are necessary for Canadian re-evaluation decisions;
- it addresses the active ingredient and the main formulation types registered in Canada; and
- it is relevant to registered Canadian uses.

Given the outcome of foreign reviews and a review of the chemistry of Canadian products, the PMRA will propose a re-evaluation decision and appropriate risk-reduction measures for Canadian uses of an active ingredient. In this decision, the PMRA takes into account the Canadian use pattern and issues (e.g. the federal Toxic Substances Management Policy [TSMP]).

Based on the health and environmental risk assessments published in the 2006 RED, the USEPA concluded that certain uses of quintozene were eligible for reregistration provided risk-reduction measures were adopted. The PMRA compared the American and Canadian use patterns and found that the USEPA assessments described in this RED were an adequate basis for the proposed Canadian re-evaluation decision.

For more details on the information presented in this overview, please refer to the Science Evaluation of this consultation document.

What Is Quintozene?

Quintozene is a fungicide that is currently used to control fungal diseases on cole crops, ornamentals and turf. As a fungicide, quintozene interferes with mitotic division and suppresses the sporulation. Quintozene can be applied by professional applicators.

Health Considerations

Can Approved Uses of Quintozene Affect Human Health?

Quintozene is unlikely to affect your health when used according to revised label directions. Additional risk-reduction measures are required on quintozene labels.

People could be exposed to quintozene by consuming food and water, working as a mixer/loader/applicator or by entering treated sites. The PMRA considers two key factors when assessing health risks: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to

assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers). Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

The USEPA concluded that quintozene was unlikely to affect human health provided that the following uses are phased-out: residential lawns, turf farms and ornamental uses (except bulb dip treatment). The USEPA's conclusions regarding residential lawns and ornamentals uses apply to the Canadian situation, and phase-out of these quintozene uses is proposed.

Maximum Residue Limits

The *Food and Drugs Act* prohibits the sale of food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in/on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Currently, quintozene is registered in Canada for use on cole crops. Quintozene could be used in other countries on crops that are imported into Canada. In Canada, the MRLs have been established for broccoli, Brussels sprouts, cabbage, cauliflower and ginseng. Where no specific MRL has been established, a default MRL of 0.1 ppm applies, which means that pesticide residues in a food commodity must not exceed 0.1 ppm. However, changes to this general MRL may be implemented in the future, as indicated in the Discussion Document DIS2006-01, *Revocation of the 0.1 ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*. If and when the general MRL is revoked, a transition strategy will be established to allow permanent MRLs to be set.

Environmental Considerations

What Happens When Quintozene Is Introduced Into the Environment?

Quintozene poses risk to non-target terrestrial and aquatic species. Additional risk-reduction measures must be observed.

Terrestrial and aquatic species could be exposed to quintozene in the environment. Environmental risk is assessed by the risk quotient method—the ratio of the estimated environmental concentration to the relevant effect's endpoint of concern. The resulting risk quotients are compared to corresponding levels of concern. A risk quotient less than the level of concern is considered a

negligible risk to non-target organisms, whereas a risk quotient greater than the level of concern indicates some degree of risk.

The USEPA concluded that the reregistration of quintozene was acceptable provided that all turf uses were terminated and that the maximum application rate on cole crops was reduced. The USEPA's conclusions apply to the Canadian situation, and equivalent risk-reduction measures are proposed.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law. As a result of the re-evaluation of quintozene, the PMRA is proposing the following.

- Reducing the maximum application rate on cole crops.
- Packaging the wettable powder formulation in water soluble packets.
- Phasing out all turf uses, including residential, commercial, turf farms and golf courses.
- Phasing out all ornamental uses except bulb dip treatment.
- Adding further protective equipment to protect mixers/loaders/applicators.
- Adding a restricted-entry interval to protect workers re-entering treated sites.
- Adding advisory label statements to protect non-target sensitive terrestrial and aquatic species.

What Additional Scientific Information Is Required?

Data to clarify current levels of impurities of toxicological concern in technical grade quintozene are required. These data have been requested from the registrant and are required under section 19 of the *Pest Control Products Act*. The registrants of this active ingredient must provide these data or an acceptable scientific rationale to the PMRA within the time line specified in the section 19 letter.

Next Steps

Before making a final re-evaluation decision on quintozene, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision[2] that will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

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2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Science Evaluation

1.0 Introduction

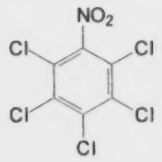
Quintozene (pentachloronitrobenzene) is an organochlorine fungicide currently registered in Canada for control of fungal diseases on cole crops, ornamentals and turf. As a fungicide, quintozene interferes with mitotic division and suppresses the sporulation.

Following the re-evaluation announcement for quintozene, the registrant of the technical grade active ingredient in Canada indicated their intention to support all quintozene uses included on the labels of commercial end-use products in Canada.

The PMRA used recent assessments of quintozene (pentachloronitrobenzene) from the USEPA. The USEPA RED document for quintozene, dated 2006, as well as other information on the regulatory status of quintozene in the United States can be found on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

Active substance	Quintozene
Function	Fungicide
Chemical names: IUPAC: CAS:	 Pentachloronitrobenzene Pentachloronitrobenzene
Chemical class:	Aromatic hydrocarbon
CAS number:	82-68-8
Molecular formula:	$C_6Cl_5NO_2$
Molecular weight:	295.34
Structural formula:	

2.2 Impurities of Concern in the Technical Grade Active Ingredient Quintozene

The following impurities of toxicological and environmental concern (DIR98-04) were present in the technical grade quintozene.

- Hexachlorobenzene—detected at the maximum level of 350 ppm
- Pentachlorobenzene—detected at the level of 100 ppm
- Total hexa- (9.3 ppb), hepta- (190 ppb) and octa- (1600 ppb) chlorodibenzo-dioxins
- Total hexa- (110 ppb), hepta- (350 ppb) and octa- (32 ppb) chlorodibenzo-furans

2.3 Physical and Chemical Properties of Quintozene

Table 3 Physical and Chemical Properties of Quintozene

Property	Result	Interpretation
Vapour pressure at 25°C	12.7 mPa	High volatility
Ultraviolet (UV)/visible spectrum	not expected to absorb at λ>300 nm	Phototransformation is unlikely
Solubility in water at 22°C	0.1 mg/L	Sparingly soluble in water
n-Octanol–water partition coefficient (K_{ow})	log K_{ow} = 5.1	Potential for bioaccumulation

2.4 Comparison of Use Patterns in Canada and the United States

Quintozene is an organochlorine used to control fungal diseases on cole crops, ornamentals and turf. It is applied as a soil treatment (cole crops, ornamentals and turf) or as a dip treatment (ornamental bulbs). The end-use products currently registered in Canada are formulated as wettable powders and suspensions. Quintozene may be applied on:

- cole crops (broccoli, Brussels sprouts, cabbage, cauliflower and other cole crops) as a transplant solution at the maximum rate of 1.97 g a.i./plant (45.4 kg a.i./ha);
- ornamentals as a dip treatment at the maximum application rate of 75 g a.i./L (7.5%) or as a soil drench, dusting or a soil incorporation at the maximum application rate of 1.5 kg a.i./100 m^2; and
- turf as a watering solution at the maximum application rate of 18.8 kg a.i./ha.

The American and Canadian use patterns were compared. At the time of the USEPA RED, quintozene for use on cole crops, turf and ornamentals was registered in both the United States and Canada. In addition, quintozene was registered in the United States for use on vegetables, field crops and as a seed treatment. Canadian use sites and end-use product formulations are encompassed by those assessed in the USEPA RED. Some of the Canadian maximum application rates are different from the American maximum application rates. The difference in the rates is discussed in more detail in the risk-assessment sections. Generally, it was concluded

that the USEPA's RED document for quintozene is an adequate basis for the re-evaluation of Canadian use of quintozene.

All current uses are being supported by the registrants and were, therefore, considered in the re-evaluation of quintozene. Appendix I lists all quintozene products that are registered as of 4 June 2008 under the authority of the *Pest Control Products Act*.

3.0 Impact on Human Health and the Environment

In their 2006 RED, the USEPA concluded that the end-use products formulated with quintozene met the safety standard under the American *Food Quality Protection Act* and would not pose unreasonable risks or adverse effects to humans and the environment if used according to the amended directions on the product labels.

3.1 Human Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels at which no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to effects of a chemical than the most sensitive animal species.

In Canada, exposure to quintozene may occur through consumption of food and water, through residential exposure, while working as a mixer/loader/applicator or by entering treated sites. The PMRA considers two key factors when assessing health risks: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers).

3.1.1 Occupational Exposure and Risk Assessment

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies being used to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating safety factors protective of the most sensitive subpopulation. If calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

The USEPA's toxicological endpoints for assessing risk from occupational exposure are summarized in Appendix II.

Workers can be exposed to quintozene when mixing, loading or applying the pesticide and when entering a treated site for the purpose of maintaining and harvesting grass.

3.1.1.1 Mixer/Loader/Applicator Exposure and Risk

Among the exposure scenarios identified in the RED document, the following 13 exposure scenarios were considered relevant to the Canadian situation.

- mixing/loading of wettable powder for cole crops treatment;
- mixing/loading of wettable powder for lawn or bulb dip treatment;
- mixing/loading of wettable powder for turf farm treatment;
- mixing/loading of wettable powder for golf course greens and tees;
- mixing/loading of wettable powder for golf course fairways;
- mixing/loading of liquid for turf farm treatment;
- mixing/loading of liquid for lawn treatment;
- mixing/loading of liquid for golf course greens and tees;
- mixing/loading of liquid for golf course fairways;
- groundboom application of wettable powder for cole crops, soil band treatment;
- high-pressure handwand spray application to lawns, commercial and residential;
- groundboom spray to turf farms; and
- mixing/loading/applying of wettable powder for ornamentals.

The USEPA determined that workers can be exposed to quintozene by the dermal and inhalation routes, while mixing/loading and/or applying the product or a combination of these activities. Separate dermal and inhalation handler exposure was estimated for different levels of protection.

The following occupational application scenarios resulted in estimated MOEs that were below the USEPA target MOE of 100 at the maximum level of protection and, therefore, were of concern:

- mixing/loading of wettable powder for turf farm treatment;
- high-pressure handwand spray application to lawns, commercial and residential; and
- mixing/loading/applying of wettable powder for ornamentals.

As a result, the American registrant proposed discontinuing use of quintozene on turf farms, residential/commercial lawns and on ornamentals (other than bulb dip treatment).

Based on the risk assessment, the USEPA required basic personal protective equipment (PPE) for mixers, loaders and other handlers of wettable powder formulation.

Relevance to the Canadian Situation
The RED adequately addressed all potential mixer/loader/applicator exposure scenarios associated with the uses of products containing quintozene in Canada but, because of the difference between Canadian and the American rates, the following was concluded.

For the mixer/loader of wettable powder for turf farm treatment, the Canadian maximum application rate is 2.4 times lower than the assessed American rate and resulted in an acceptable MOE. Consequently, the USEPA conclusion that this scenario is of concern is not applicable to the Canadian rate.

The Canadian maximum application rate on cole crops (45.4 kg a.i./ha) is 1.35 times higher than the assessed American maximum application rate (33.7 kg a.i./ha). The inhalation MOE of 120 for the mixer/loader of wettable powder, at the highest level of protection, does not provide sufficient protection to account for the difference in application rate between the United States and Canada.

Therefore, based on conclusions regarding a mixer/loader/applicator risk in the RED document, the PMRA proposes the following.

- Reducing the maximum application rate on cole crops (transplant solution).
- Phasing out quintozene use on residential and commercial lawns.
- Phasing out wettable powder use on ornamentals except a bulb dip treatment.
- Packaging the wettable powder products in water soluble packets.
- Requiring that a long-sleeved shirt, long pants, shoes plus socks and chemical-resistant gloves should be worn when handling the product. In addition, a chemical-resistant apron and a National Institute of Occupational Safety and Health (NIOSH)-approved respirator are required for workers involved in bulb soaking applications.

3.1.1.2 Postapplication Exposure and Risk

The USEPA determined there is a low potential for occupational postapplication exposure when quintozene is applied as a transplant solution during seedling planting. Therefore, a postapplication assessment for agriculture use was not required.

The USEPA performed a risk assessment for the scenario associated with the highest potential for postapplication exposure, i.e. individuals re-entering quintozene treated areas for the purpose of turf-grass maintenance and harvesting. The assessment was based on a maximum application rate of 46 kg a.i./ha on turf. Resulting MOEs were not of concern and no mitigation measures were required by the USEPA.

As per the United States Worker Protection Standard, the USEPA required a restricted-entry interval of 12 hours to protect postapplication workers.

The RED adequately addressed potential exposure scenarios associated with the Canadian uses of quintozene, and the USEPA's conclusions are considered to be applicable to the Canadian situation. A restricted-entry interval of 12 hours is being proposed to be added to the Canadian label for agricultural use. The proposed label amendment is listed in Appendix III.

3.1.2 Non-Occupational Exposure and Risk Assessment

3.1.2.1 Residential Exposure

There are no domestic class end-use products containing quintozene registered in Canada; therefore, only residential postapplication exposure to quintozene treated lawns was considered in this review. The toxicological endpoints selected by the USEPA for assessment of risk from residential exposure are summarized in Appendix II.

The USEPA assessed the following scenarios of postapplication exposure from treated turf:

- oral non-dietary exposure of toddlers (ingestion of soil, hand-to-mouth and object to mouth activity);
- dermal exposure of toddlers and adults to treated lawns (playing on lawn, mowing the grass); and
- golfers re-entering a quintozene treated golf course.

Based on the risk assessment the USEPA determined the following.

- The MOEs associated with oral non-dietary exposure of toddlers (MOEs ranging from 1–612) or with dermal exposure of toddlers and adults to treated turf (MOE of 40 and 110, respectively) were below the USEPA's target MOE of 1000.
- Postapplication risk to adults mowing the grass (MOE of 1145) and to golfers re-entering treated sites (MOEs ranging from 3100 to 4100) was not of concern.

As a result, the American registrants voluntarily cancelled all residential turf uses.

Relevance to the Canadian Situation
The Canadian maximum application rate (18.8 kg a.i./ha) is 1.9 times lower than the assessed American rate (36 kg a.i./ha). The PMRA found that some of the USEPA's MOEs associated with oral non-dietary (hand-to-mouth and object to mouth activity) and dermal contact exposure (toddlers and adults) still represent a concern, and the USEPA's conclusions are considered relevant to the Canadian situation. Therefore, quintozene use on residential turf is proposed for phase-out in Canada.

3.1.2.2 Exposure From Food and Drinking Water

No toxicological endpoint attributed to a single oral dose was identified in available toxicological studies on quintozene. Therefore, no acute dietary risk assessment for quintozene was performed by the USEPA.

A chronic dietary risk is estimated by determining how much of a pesticide residue may be ingested with the daily diet and comparing this potential exposure to an acceptable daily intake, which is the dose at which an individual could be exposed over the course of a lifetime and expect no adverse health effects. The acceptable daily intake is referred to as the ADI in Canada, and, in the RED, it is expressed as the chronic population-adjusted dose (cPAD). The ADI is based on a relevant endpoint from toxicology studies and on safety factors protective of the most sensitive subpopulation.

The USEPA's highly refined chronic dietary risk assessment was based on a reduced application rate on cole crops (25.3 kg a.i./ha) and used all available monitoring data and information on percentage of crops treated. The chronic risk assessment resulted in risk estimates below 100% of the cPAD for the general population and all subgroups. The highest estimated exposure, from food only, was for children 1–2 years of age, utilizing 34% of the cPAD.

The USEPA determined that surface water sources were more likely to be contaminated with quintozene than groundwater sources, because quintozene was found to be relatively immobile in soils. Quintozene may reach surface water through drift when applied as a spray, particularly with foliar applications (such as turf). Screening models were used to estimate quintozene concentrations in the ground and surface water. The estimated drinking water concentration (EDWC) from ground water sources was 30.6 ppb. The estimated drinking water concentrations from surface water were 88.8 ppb and 10.3 ppb for acute and chronic exposures, respectively. When water was added to the dietary risk analysis, the exposure was estimated to take up 79% of the cPAD for the most sensitive population subgroup, infants (less than one year old).

Cancer dietary exposure assessment was not required because quintozene was classified as an unquantified Group C (possible human) carcinogen, with a threshold effect observed in test animals. There was no concern for mutagenicity resulting from exposure to quintozene.

The USEPA's assessment encompassed Canadian registered uses of quintozene and is considered applicable to the Canadian situation.

3.1.2.3 Aggregate Risk Assessment

The aggregate risk assessment conducted by the USEPA included dietary exposure (food and water) only because the risk associated with postapplication activities was of concern and residential uses on turf has been cancelled voluntarily by the American registrant. The aggregated exposure to quintozene residues in/on food and water represented 79% of the cPAD for the most sensitive population subgroup, infants (less than one year old).

Overall, the Canadian aggregate exposure scenario was adequately addressed by the USEPA aggregate risk assessment, and the USEPA aggregate exposure conclusions are considered applicable to quintozene uses in Canada, provided that residential turf uses are phased out.

3.1.3 Cumulative Effects

The USEPA has not determined whether quintozene has a common mechanism of toxicity with other substances or whether it shares a toxic metabolite produced by other substances. Therefore, it was assumed that quintozene does not share a common mechanism of toxicity with other substances and a cumulative risk assessment was not required.

3.2 Environment

3.2.1 Fate Characteristic

The USEPA determined the following.

- Quintozene was found to be very persistent in the environment, with aerobic and an anaerobic soil metabolism half-life of 189 and 30 days, respectively.

- Quintozene was found to be immobile in most soils, but potentially able to partition to organic matter in the soils and move to surface water through erosion. Therefore, the surface water was found more likely to be contaminated.

- Quintozene was found to be stable to hydrolysis and stable to photodegradation on soil. Photodegradation in surface water was moderately rapid, with a half-life up to 2.5 days.

- The bioconcentration factor of 1100 times was reported for fish. Higher bioconcentration factor was reported for aquatic plants, up to 3100 times for algae. The log n-octanol–water coefficient factor (K_{ow}) is 5.1. The results indicated that quintozene and its transformation products (including pentachloroaniline, pentachlorobenzene and pentachlorothioanisole) display high potential to accumulate in aquatic organisms.

- Quintozene was found to be highly volatile with a vapour pressure of 12.7 mPa at 25°C. It was determined that a significant amount of quintozene could volatilize from the soil and undergo long-range transport. Residues of quintozene have been detected in regions where the product was never used, e.g. Saskatchewan. The USEPA reported a photo-oxidation half-life of 2200 days for quintozene.

- Quintozene was found to contain high levels of the manufacturing contaminant hexachlorobenzene, which was also reported as a transformation product in field dissipation and anaerobic aquatic metabolism studies.

- Quintozene was found to meet the criteria of the persistent bioaccumulative and toxic substances established by the USEPA. It persists in the environment (half-life in soil >60 days), accumulates in human and other species (bioconcentration factor >1000 days) and is toxic to fish and invertebrates on acute exposure basis.

3.2.2 Environmental Risk Assessment

To assess the ecological risk of quintozene to both terrestrial and aquatic non-target plants and animals, the USEPA calculated risk quotients (RQs) based on appropriate toxicity endpoints and expected environmental concentrations (EECs) and compared the resulting RQs to corresponding levels of concern (LOCs).

The USEPA environmental risk was based on the maximum application rate on turf (48.7 kg a.i./ha) and cabbage (25.3 kg a.i./ha, a reduced application rate proposed by the American registrant). The USEPA determined the following.

- For quintozene application on turf, the acute LOCs were exceeded for mammals (RQs of 0.58 to 3.7), freshwater fish (RQ of 2.6) and estuarine/marine invertebrates (RQ of 22). However, the chronic LOCs were exceeded for birds (RQs of 2 to 33), mammals (RQs of 4 to 1858), and freshwater fish and invertebrates (RQs of 8.2 and 5.9, respectively).

- For quintozene application on cabbage, the acute LOCs were exceeded for intermediate birds feeding on short grass (RQ of 0.88); large birds feeding on short grass, tall grass and broadleaf plants/small insects (RQs of 1.8 to 3.9); and for estuarine/marine invertebrates (RQ of 3.03). However, the chronic LOCs were exceeded for all size birds feeding on all food types, except fruits/pods/seeds/large insects, (RQs of 4.1 to 9), and for all size mammals (RQs of 1.5 to 234).

No chronic toxicity data were available for estuarine/marine animals; however, given estuarine/marine organisms were more sensitive to quintozene on an acute basis than their freshwater counterparts, the USEPA determined that they would be also more sensitive on a chronic basis.

The USEPA determined the following.

- Quintozene use on cole crops to control clubroot only was eligible for continued registration.

- Turf uses (both residential and commercial) were not eligible for continued registration.

Relevance to the Canadian Situation
The American use pattern for quintozene generally encompasses the Canadian use pattern. Although the Canadian maximum application rate on turf is 2.6 times lower than the American rate, the risk to mammals and birds would still remain of concern. Therefore, the USEPA's assessment and conclusions are considered relevant to the Canadian situation and the following mitigation measures are proposed by the PMRA:

- reducing maximum seasonal applications rate to cole crops from 45.4 kg ai/ha (1.97 g a.i./plant) to 25.3 kg a.i./ha (1.1 g ai/plant);

- phasing out all turf uses including residential lawn, industrial/commercial turf, turf farms and all golf course turf; and
- adding precautionary statements pertaining to the environmental hazard to all quintozene end-use product labels. Proposed label amendments are listed in Appendix III.

The PMRA is currently developing a policy for managing chemicals that are persistent, bioaccumulative and toxic. Quintozene is considered to have persistent bioaccumulative and toxic characteristics and will be revisited once an approach has been developed.

3.2.3 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the 1995 federal TSMP, which puts forward a preventive and precautionary approach to deal with substances that enter the environment and could harm the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track 1 substances.

The federal TSMP and PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, were taken into account during the re-evaluation of quintozene, which led to the following conclusions.

- By definition, the majority of chemical pesticides are considered to arise from anthropogenic sources as they are manufactured and applied to the environment for pest control purposes. As such, quintozene is considered to have met the criteria of being predominately anthropogenic.

- Quintozene was observed to have an aerobic soil half-life of 189 days, exceeding the TSMP persistence criteria of six months.

- Quintozene vapour phase $t_{1/2}$ of 2200 days exceeds the TSMP Track 1 long-range transport criterion of a half-life greater than two days in air.

- The quintozene *n*-octanol–water partition coefficient (log K_{ow}) of 5.1 reported by the PMRA exceeds the TSMP criterion of 5. However, the bioconcentration factor of 1100 times for whole fish and 3100 times for algae reported in the RED document is lower than the TSMP criterion of 5000. Therefore, quintozene is not a candidate for Track 1 classification.

- Quintozene is considered to have persistent bioaccumulative and toxic characteristics. The PMRA is currently developing a policy for managing persistent bioaccumulative and toxic chemicals, and quintozene will be revisited once an approach has been developed. Analysis of batch samples of technical grade quintozene previously submitted to PMRA revealed presence of hexachlorobenzene at the level at 350 ppm, pentachlorobenzene at the level of 100 ppm and low levels of dioxins/furans (total hexa-, hepta- and octa- chlorodibenzo-dioxins and furans at the maximum levels of 9.3 and 110 ppb, 190 and 350 ppb, 1600 and 32 ppb, respectively). Dioxins/furans and chlorinated benzenes have been identified in the federal government's TSMP as Track 1 substances. Analyses of recent production batches of the technical grade quintozene using sensitive and readily available analytical methods are required from the registrant.

- No other impurities of toxicological concern as identified in Regulatory Directive DIR98-04, Section 2.13.4, or TSMP Track1 substances as identified in Regulatory Directive DIR99-03, Appendix I, are expected to be present in the technical product of quintozene.

Formulant issues are being addressed through PMRA formulant initiatives and Regulatory Directive DIR2006-02, *Formulants Policy and Implementation Guidance Document,* published on 31 May 2006.

4.0 OECD Status of Quintozene

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which groups 30 member countries and provides governments with a setting in which to discuss, develop and perfect economic and social policies. They compare experiences, share information and analyses, seek answers to common problems, and work to co-ordinate domestic and international policies to allow for consistency in practices across nations.

Based on the current available information on the status of quintozene in the OECD member countries, it was found that quintozene was prohibited due to health and/or environmental concerns in Sweden (1985),[3] Finland (1996),[4] the Republic of Korea (1987; PIC circular X),[5] Germany (1988; PIC circular X),[5] Austria (1992; PIC circular X),[5] Switzerland (1992; PIC circular XX).[5] In 2000, due to concerns of the risk to human health, persistence in

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3 Swedish Chemicals Agency's Regulations on Chemical Products and Biotechnical Organisms (KIFS 1998:8) Appendix 5.

4 Finish Food Safety Authority EVIRA.

5 Prior informed consent (PIC) circulars are published by the Rotterdam Convention Secretariat. Under this Convention, parties to the Convention have committed to inform other parties about legislative bans or severe restrictions on the use of chemicals and to notify recipient countries of any exports of regulated substances. This procedure is called Prior Informed Consent (PIC). When a party has adopted a final regulatory action to ban or severely restrict a chemical, the party notifies the Rotterdam Convention Secretariat; notifications are published in PIC circulars.

the environment and possible impact on non-target organisms, quintozene products were prohibited by the European Union.[6] In 2006, based on the concerns for human health and the environment, the United States, also an OECD member, found quintozene use on turf and ornamentals (except bulb dip) not eligible for re-registration.

The Canadian re-evaluation of quintozene is largely based on the 2006 USEPA assessment. The PMRA has found the USEPA's conclusions, pertaining to human health and environmental risk, to be relevant to quintozene use in Canada. The same measures to reduce potential risk to human health and environment are proposed by the PMRA.

The concerns identified in the OECD countries relating to human health and environmental risk associated with quintozene was taken into consideration in the re-evaluation of quintozene in Canada and have been addressed in the proposed Canadian re-evaluation decision.

5.0 Proposed Re-evaluation Decision

After a re-evaluation of the fungicide quintozene, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration of certain products containing quintozene for the sale and use in Canada.

Products containing quintozene used on cole crops and for ornamental bulb dip do not pose unacceptable risk to human health or the environment and have value for agriculture when used according to the label directions. As a condition for continued registration of quintozene products, the following new risk-reduction measures will be required.

- Reduce the maximum application rate of a quintozene on cole crops, applied as a transplant solution, to 1.1 g a.i./plant (equals to 25.3 kg a.i./ha).

- Package wettable powder products in water soluble packets.

Certain uses of quintozene are proposed for phase-out because the risk associated with these uses exceeded current health and environmental standards. They include all products for turf and ornamental uses (except bulb dip treatment).

The PMRA is currently developing a policy for managing chemicals that are persistent, bioaccumulative and toxic (persistent bioaccumulative and toxic). Quintozene is considered to have persistent bioaccumulative and toxic characteristics and will be revisited once an approach has been developed.

Further measures may be necessary pending the outcome of the TSMP assessment regarding the impurities of toxicological concerns.

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[6] European Union Directive 79/117/EEC (1991) (00/816) Regulatory Decision excluding substances from Annex I of Directive 91/414.

6.0 Data Required as a Condition of Continued Registration

Additional data regarding impurities of toxicological concern have been requested from the registrant and are required under section 19 of the *Pest Control Products Act*.

7.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2001-03, and data code (DACO) tables can be found on our website at www.hc-sc.gc.ca/cps-spc/pest/index-eng.php. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra_infoserv@hc-sc.gc.ca.

The federal TSMP is available through Environment Canada's website at www.ec.gc.ca/toxics.

The USEPA RED document for quintozene (pentachloronitrobenzene) is available on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

List of Abbreviations

ADI	acceptable daily intake
a.i.	active ingredient
bw	body weight
CAS	Chemical Abstracts Service
cPAD	chronic population adjusted dose
DACO	data code
EEC	expected environmental concentration
FQPA	*Food Quality Protection Act*
g	gram(s)
ha	hectare
kg	kilogram(s)
K_{ow}	*n*-octanol–water partition coefficient
L	litre(s)
LOAEL	lowest observed adverse effect level
LOC	level of concern
LOD	limit of detection
m	metre(s)
MOE	margin of exposure
MRL	maximum residue limit
NIOSH	National Institute of Occupational Safety and Health
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
PHED	Pesticide Handlers Exposure Database
PMRA	Pest Management Regulatory Agency
ppb	parts per billion
PPE	personal protective equipment
ppm	parts per million
PRVD	Proposed Re-evaluation Decision
RED	Reregistration Eligibility Decision
RVD	Re-evaluation Decision
RQ	risk quotient
TSMP	Toxic Substances Management Policy
UF/SF	uncertainty factor/safety factor
USEPA	United States Environmental Protection Agency
UV	ultraviolet

Appendix I Registered Products Containing Quintozene as of 4 June 2008

Registrant Number	Marketing class	Registrant	Product Name	Formulation Type	Guarantee
07251	Commercial	Amvac Chemical Corporation	Quintozene (Terraclor®) 75%WP	Wettable powder	75%
11425	Commercial	Plant Products Co. Ltd.	Quintozene 75% WP Fungicide	Wettable powder	75%
23334	Technical	Amvac Chemical Corporation	Technical Grade Quintozene	Dust or powder	96.2%
27212	Technical	Amvac Chemical Corporation	Quintozene (Terraclor®) Technical	Dust or Powder	96.2%
27416	Commercial	Amvac Chemical Corporation	Quintozene 75 WP Soil Fungicide	Wettable powder	75%
27691	Commercial	Amvac Chemical Corporation	Terraclor® Flowable Fungicide	Flowable suspension	40%
28238	Commercial	Chemtura Canada Co./Cie	CRUSOE™ 75 WP Soil Fungicide	Wettable powder	75%
28663	Commercial	Chemtura Canada Co./Cie	ADOBE 75WP Fungicide, Soil Fungicide	Wettable powder	75%

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23334	Technical	Amvac Chemical Corporation	Technical Grade Quintozene	Dust or powder	96.2%
27212	Technical	Amvac Chemical Corporation	Quintozene (Terraclor®) Technical	Dust or Powder	96.2%
27416	Commercial	Amvac Chemical Corporation	Quintozene 75 WP Soil Fungicide	Wettable powder	75%
27691	Commercial	Amvac Chemical Corporation	Terraclor® Flowable Fungicide	Flowable suspension	40%
28238	Commercial	Chemtura Canada Co./Cie	CRUSOE™ 75 WP Soil Fungicide	Wettable powder	75%
28663	Commercial	Chemtura Canada Co./Cie	ADOBE 75WP Fungicide, Soil Fungicide	Wettable powder	75%

Appendix II Toxicological Endpoints Selected by the USEPA for Quintozene Health Risk Assessments

Exposure Scenario	Dose Used In Risk Assessment (FQPA Safety Factor)	Study and Toxicological Effects	Level of Concern for Risk Assessment
Acute Dietary	N/A	None selected	N/A
Chronic Dietary	Oral NOAEL= 1.0 mg/kg/day (10×) cPAD 0.001 mg/kg/day	Chronic/oncogenicity (rat), LOAEL 150 mg/kg bw/day based on hepatocellular hypertrophy and hyperplasia, thyroid hypertrophy	≤100% of cPAD
Short-Term Incidental Oral	Oral NOAEL < 1.0 mg/kg/day (10×)	90- day subchronic (rat) LOAEL 1 mg/kg bw/day based on no toxicity at 30d	MOE* ≥1000
Intermediate-Term Incidental Oral	Oral NOAEL < 1.0 mg/kg/day (10×)	90- day subchronic (rat) LOAEL 1.0 mg/kg bw/day based on threshold effects (liver and thyroid lesions) seen at the lowest dose tested	MOE ≥1000
Short- and Intermediate-Term Dermal	NOAEL= 300 mg/kg/day (10×, residential)	21- day dermal study (rat) LOAEL 1000 mg/kg bw/day based on hypertrophy of thyroid follicular epithelium and dilation of thyroid follicles in males	Resid. MOE ≥1000 Occup. MOE >100
Long-Term Dermal	Oral NOAEL= 1.0 mg/kg/day; dermal absorption 33% of oral	Chronic/oncogenicity (rat) LOAEL 150 mg/kg bw/day based on hepatocellular hypertrophy and hyperplasia, thyroid hypertrophy	MOE ≥100
Short-Term Inhalation	Oral NOAEL < 1.0 mg/kg/day (10×, residential); inhalation absorption 100% of oral	90- day subchronic (rat) LOAEL 1.0 mg/kg bw/day based on no toxicity at 30 days	Resid. MOE ≥1000 Occup. MOE >100
Intermediate-Term Inhalation	Oral NOAEL < 1.0 mg/kg/day (10×, residential) inhalation absorption 100% of oral	90- day subchronic (rat) LOAEL 1 mg/kg bw/day based on threshold effects (liver and thyroid lesions) seen at the lowest dose tested	Resid. MOE ≥1000 Occup. MOE ≥100
Long-Term Inhalation	Oral NOAEL= 1.0 mg/kg/day inhalation absorption 100% of oral absorption	Chronic/ oncogenicity (rat) LOAEL 150 mg/kg bw/day based on hepatocellular hypertrophy and hyperplasia, thyroid hypertrophy	MOE ≥100
Cancer	Quintozene is classified as a Group C (possible human) carcinogen. For the purpose of risk characterization, the chronic dietary risk assessment approach is used to quantify cancer risk.		

* MOE refers to a desired margin of exposure for occupational or residential assessments.

Appendix II Toxicological Endpoints Selected by the USEPA for Quintozene Health Risk Assessments

Exposure Scenario	Dose Used In Risk Assessment (FQPA Safety Factor)	Study and Toxicological Effects	Level of Concern for Risk Assessment
Acute Dietary	N/A	None selected	N/A
Chronic Dietary	Oral NOAEL= 1.0 mg/kg/day (10×) cPAD 0.001 mg/kg/day	Chronic/oncogenicity (rat), LOAEL 150 mg/kg bw/day based on hepatocellular hypertrophy and hyperplasia, thyroid hypertrophy	≤100% of cPAD
Short-Term Incidental Oral	Oral NOAEL < 1.0 mg/kg/day (10×)	90- day subchronic (rat) LOAEL 1 mg/kg bw/day based on no toxicity at 30d	MOE* ≥1000
Intermediate-Term Incidental Oral	Oral NOAEL < 1.0 mg/kg/day (10×)	90- day subchronic (rat) LOAEL 1.0 mg/kg bw/day based on threshold effects (liver and thyroid lesions) seen at the lowest dose tested	MOE ≥1000
Short- and Intermediate-Term Dermal	NOAEL= 300 mg/kg/day (10×, residential)	21- day dermal study (rat) LOAEL 1000 mg/kg bw/day based on hypertrophy of thyroid follicular epithelium and dilation of thyroid follicles in males	Resid. MOE ≥1000 Occup. MOE >100
Long-Term Dermal	Oral NOAEL= 1.0 mg/kg/day; dermal absorption 33% of oral	Chronic/oncogenicity (rat) LOAEL 150 mg/kg bw/day based on hepatocellular hypertrophy and hyperplasia, thyroid hypertrophy	MOE ≥100
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Intermediate-Term Inhalation	Oral NOAEL < 1.0 mg/kg/day (10×, residential) inhalation absorption 100% of oral	90- day subchronic (rat) LOAEL 1 mg/kg bw/day based on threshold effects (liver and thyroid lesions) seen at the lowest dose tested	Resid. MOE ≥1000 Occup. MOE >100
Long-Term Inhalation	Oral NOAEL= 1.0 mg/kg/day inhalation absorption 100% of oral absorption	Chronic/ oncogenicity (rat) LOAEL 150 mg/kg bw/day based on hepatocellular hypertrophy and hyperplasia, thyroid hypertrophy	MOE ≥100
Cancer	Quintozene is classified as a Group C (possible human) carcinogen. For the purpose of risk characterization, the chronic dietary risk assessment approach is used to quantify cancer risk.		

* MOE refers to a desired margin of exposure for occupational or residential assessments.

Appendix III Label Amendments for Products Containing Quintozene

The label amendments presented below do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Additional information on labels of currently registered products should not be removed unless it contradicts the above label statements.

A submission to request label revisions will be required within 90 days of finalization of the re evaluation decision.

The labels of end-use products in Canada must be amended to include the following statements to further protect workers and the environment.

I) The following uses are not eligible for continued registration and must be removed from end-use product labels:

- all turf uses including residential and commercial lawns, turf farms, golf courses; and
- ornamental uses, with the exception of bulb dip treatment.

II) The end-use product label must be amended to indicate a maximum application rate on cole crops, as a transplant solution, of 1.1 g ai/plant, as follows.

> Use 1–1.5 kg per 400 L of water, apply maximum of 400 mL per plant for cole crop transplant solution application.

III) The following statements must be included in a section entitled **DIRECTIONS FOR USE**.

> Quintozene is a dry powder sealed within a water soluble bag. Drop an intact water soluble bag directly into a mixing tank. The water soluble bag and pesticide will dissolve readily in water.
>
> Do not allow the water soluble bag to become wet prior to use. Do not remove a water soluble bag from an overwrap container except for immediate use.
>
> Do not open or puncture a water soluble bag for any reason.
>
> If a broken water soluble bag is found when the overwrap bag is opened, avoid contact with, and inhalation of the product.

IV) The following statements must be included in a section entitled **STORAGE**.

> Store in cool, dry, well-ventilated place. Do not remove the pouch from an overwrap container except for immediate use. Do not allow to become wet in storage. Keep the container closed when not in use.

VI) The following statements must be included in a section entitled **PRECAUTIONS.**

A long-sleeved shirt and long pants, shoes plus socks and chemical-resistant gloves should be worn when handling the product. In addition, a chemical-resistant apron and NIOSH-approved respirator are required for workers involved in bulb soaking applications.

Do not enter or allow workers entry into treated areas for 12 hours following application.

VII) The following statement must be included in a section entitled **ENVIRONMENTAL HAZARDS.**

Toxic to aquatic organisms, birds and small wild mammals

To reduce runoff from treated areas into aquatic habitats avoid application to areas with a moderate to steep slope, compacted soil, or clay.

Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body.

Avoid application when heavy rain is forecast.

To minimize the release of quintozene into the environment due to volatilization, quintozene should only be applied on cool mornings and evenings when air temperatures are 15°C or lower. To further reduce volatilization to the atmosphere, incorporation into the soil should occur concurrently with application.

DO NOT apply this product directly to freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands), estuarine/marine habitats.

DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.

References

Studies considered in the Chemistry Assessment

A. LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

PMRA Document Number	References
1480195	Specifications and Analytical Methodology for Pentachloronitrobenzene (PCNB). Vol. 3 QTZ-AMV-1, DACO: 2.1,2.10,2.14,2.2,2.3,2.4,2.5,2.6,2.7,2.8,2.9; DACO 2.14
1480169	TGAI Chemistry. QTZ-AMV-1, DACO: 2.99; DACO 2.14, DACO 2.11
1480199	1993, Specifications and Analytical Methodologies for Pentachloronitrobenzene (PCNB). Supplemental Data in Response to Letter of March 24, 1993., DACO: 2.13.3
1480183	Specifications and Analytical Methodology for Pentachloronitrobenzene (PCNB). Vol. 4 QTZ-AMV-1, DACO: 2.11.1,2.11.2,2.12,2.13.1,2.13.4
1480198	1992, Specifications and Analytical Methodologies for Pentachloronitrobenzene (PCNB). Supplemental Data in Response to Letter of April 28, 1992., DACO: 2.13.4
1480201	2002, Response to Clarification Notice: Quintozene 75 WP (Sub. # 1996-0190). Response toYour Clarification Notice Dated November 28, 2002., DACO: 2.13.4